Bone Marrow Cells Are Able to Generate Prostatic Epithelial and Stromal Cells

Xiaozhong Xiong[1,*], Ken Goto[1,4], Yasuhiro Ebihara[3], Sarah Salm[1,5], Sandra Coetzee[1], Christopher Ontiveros[1], David Moscatelli[1], Makio Ogawa[3], and E. Lynette Wilson[1,2]

[1]Department of Cell Biology, New York University School of Medicine, New York, NY
[2]Department of Urology, New York University School of Medicine, New York, NY
[3]Department of Veterans Affairs Medical Center, Medical University of South Carolina, Charleston, SC
[4]Department of Urology, Graduate School of Medical Sciences, Kyushu University, Fukuoka Japan
[5]Borough of Manhattan Community College, New York, NY

Recent studies have shown that adult bone marrow-derived stem cells maintain plasticity and can differentiate into tissues of multiple organs. It therefore appears that a number of organs are capable of repairing themselves either from stem cells located within the organ or from cells recruited from the bone marrow. We therefore determined whether bone marrow (BM) cells are capable of differentiating into prostatic cells using *in vitro* and *in vivo* methodology. We show that unfractionated BM cells can differentiate into prostate epithelial cells when bone marrow cells are cultured with regenerating prostate cells in trans-well dishes separated by a membrane. We determined the expression of the prostate specific protein, probasin, and the epithelial marker, cytokeratin 19 (CK 19), by RT-PCR 48 and 96 hours after co-culture. We find that BM cells express probasin and CK19 within 48 hours of co-culture. After 96 hours of co-culture the expression of probasin and CK19 is further increased by 2.8 fold and 3.2 fold of the expression noted at 48 hours. These results indicate that regenerating prostatic tissue produces factors that induce BM cells to differentiate into prostatic epithelial cells.

To determine if BM cells can differentiate into prostate cells *in vivo*, we reconstituted lethally irradiated host animals with GFP-expressing BM cells and examined prostatic tissue for evidence of GFP-expressing cells. To enhance incorporation of BM cells into prostatic tissue, we subjected the transplanted animals to multiple cycles (3-7 cycles) of prostatic involution and regeneration by withdrawing and adding androgens to castrated animals. GFP-expressing cells were found within the prostatic epithelial (1.52 ± 0.02%) and stromal compartments (4.41 ± 0.7%). Because BM cells express CD45, we then determined the fraction of GFP positive cells that lacked CD45 expression. We found that 65% of GFP-expressing cells in the epithelial layer and 50% of the GFP-expressing cells in the stromal compartment lacked CD45. Most of the GFP-expressing cells in the epithelial compartment were found in the basal cell layer, with some of these cells co-expressing both GFP and CK 5 (a CK expressed by basal cells). Similarly, some of the GFP-expressing cells in the stromal compartment co-expressed markers of stromal cells (vimentin and α-smooth muscle actin).

These data indicate that cells of BM origin can differentiate into prostatic cells of both epithelial and stromal origin and may be relevant in the etiology of prostatic proliferative diseases such as benign prostatic hyperplasia and prostatic carcinoma.

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